

Remarks

Claims 16-55, 81 and 82 are pending.

§ 103 Rejection over Boyer

Claims 16-25, 32-34, 36-45, 52-54, 81 and 82 are rejected under 35 U.S.C. § 103 as being obvious over Boyer (U.S. Patent No. 4,800,079).

Applicants respectfully traverse the rejection and respectfully submit that Boyer does disclose or suggest the claimed fenofibrate to polymer ratio of between 1:10 and 4:1 as recited in independent claims 16 and 36.

Boyer discloses a composition containing micronized fenofibrate, a polymer such as polyvinylpyrrolidone (PVP), and possibly starch. The sole example that is provided in Boyer¹ comprises 400 kg of fenofibrate and 20 kg of PVP and/or methacrylate. As correctly pointed out by the U.S. Patent Office (PTO), Boyer's ratio of fenofibrate to polymer is 20:1. Boyer does not provide any motivation or suggestion to drastically reduce the weight ratio of fenofibrate to PVP of 20:1 to be any where near the claimed range of fenofibrate to polymer of between 1:10 and 4:1. The weight ratio in Boyer is significantly different than the claimed weight ratio and there is no motivation or suggestion to arrive at the claimed weight ratio of between 1:10 and 4:1. The ratio of fenofibrate to polymer in Boyer has more than 5 times fenofibrate to PVP than the claimed ratio of fenofibrate to polymer.

One skilled in the art could not use routine experimentation to arrive at the claimed ratio because it would require one to drastically reduce Boyer's ratio to be 5 times less than stated to arrive at the claimed invention. Routine variation or experimentation would revolve around Boyer's ratio of 20:1, and not the claimed ratio that is 5 times smaller. In view of the significant difference in the ratios, the claimed ratio is not encompassed by Boyer and is not merely an optimization of the ratio described by Boyer.

The PTO asserts that Applicants failed to show the criticality of the claimed ratio. Applicants respectfully disagree that such a showing is necessary for patentability. The case law cited by the PTO² requires that the general conditions of a claim be disclosed in the prior art. In

¹ Boyer at column 3.

² *In re Aller*, 220 F.2d 454 (1955).

the present case, the claimed ratios are not a variation of or encompassed by the prior art. The claimed ratios are significantly different than the ratios recited in Boyer. In view of the above, Applicants respectfully submit that the PTO has not established a *prima facie* case of obviousness.

Although the criticality of the claimed range is not required because the PTO has not established a *prima facie* case of obviousness, Applicants have provided data showing the criticality of the claimed range, as discussed below.

The dissolution medium and conditions in the present claims are a rotating blade method at 75 rpm, where the dissolution medium is water with 2% polysorbate 80 or water with 0.025 M sodium lauryl sulfate. In contrast, Boyer uses 35 ml of a medium having a pH of 1.5, and a stirring speed of 30 rpm at 37°C. Having a different pH and rotating speed will influence dissolution. Accordingly, it is necessary to compare the composition described in Boyer and the claimed composition using the same method.

In support of the fact that the invention provides unexpectedly superior results over Boyer, Applicants refer to the Declaration under 37 C.F.R. § 1.132 by Philippe Reginault (hereafter the Reginault Declaration) attached hereto and submitted in the related case of US Application No. 10/288,425. The Reginault Declaration provides a direct comparison between Boyer and the claimed invention.

It is known in the art that the composition described by Boyer is represented by Lipanthyl® 250. *See* Reginault Declaration at ¶ 7.

The composition recited in the claims is represented in the specification at Example 2 and by Lipanthyl® Supra. *See* Reginault Declaration at ¶ 8.

A comparison of the dissolution profile of Boyer (i.e., Lipanthyl® 250) and the claimed invention (i.e., Lipanthyl® Supra) is shown in Tables 1 and 2 and Figures 1 and 2 in the Reginault Declaration at ¶ 11.

For the Examiner's convenience, the results described in the Reginault Declaration and shown in Example 2 and Figure 1 in the present application are reproduced in the Table below.

Time	% Dissolution as disclosed in the Present Invention	% Dissolution of Lipanthyl® 250 corresponding to Boyer	% Dissolution of Lipanthyl® Supra corresponding to the Claimed Invention	% Dissolution of Inventive Example 2 in the Application
5 minutes	at least 10%	0.4%	26.8%	18.9%
10 minutes	at least 20%	0.8%	60.5%	67.1%
20 minutes	at least 50%	1.2%	83.0%	89.7%
30 minutes	at least 75%	1.9%	89.8%	95.9%

In comparing Boyer and the claimed invention, the Reginalt Declaration, at ¶ 12, states:

The results shown above clearly demonstrate that Lipanthyl® 250 (i.e., U.S. Patent No. 4,800,079 to Boyer) and Lipanthyl® Supra (i.e., the above-identified application) have very different dissolution profiles — both for the extent and for the rate. Lipanthyl® Supra presented a complete dissolution of fenofibrate within 1 hour whereas Lipanthyl® 250 only released 4% fenofibrate (i.e., 10 mg) within 1 hour. Hence, the two formulations have a significantly different dissolution profiles.

As shown in the Reginalt Declaration at ¶ 13 and the specification at Example 2, the presently claimed invention has an unexpectedly superior dissolution profile when compared to Boyer. Accordingly, one skilled in the art would not arrive at the presently claimed invention based on the teachings in Boyer.

Applicants respectfully submit that pending claims 16-25, 32-34, 36-45, 52-54, 81 and 82 are unobvious over Boyer because the PTO has not established a *prima facie* case of obviousness and Applicants have shown the criticality of the claimed range; and respectfully request that the rejection under § 103 be withdrawn.

§ 103 Rejection over Curtet

Claims 16-55, 81 and 82 are rejected under 35 U.S.C. § 103 as being obvious over Curtet et al (U.S. Patent No. 4,895,726).

Applicants respectfully traverse the rejection and respectfully submit that Curtet does disclose or suggest the claimed fenofibrate to polymer ratio of between 1:10 and 4:1, as recited

in independent claims 16 and 36.

Curtet provides working examples comprising 200 grams fenofibrate and 7 grams cross-linked polyvinylpyrrolidone,³ such that the weight ratio of fenofibrate to cross-linked polyvinylpyrrolidone is 29:1. Curtet does not provide any motivation or suggestion to drastically reduce the weight ratio of fenofibrate to polyvinylpyrrolidone (PVP) of 29:1 to the claimed range of fenofibrate to polymer of between 1:10 and 4:1. The weight ratio in Curtet is significantly different than the claimed weight ratio and there is no motivation or suggestion in any of the references to arrive at the claimed weight ratio of between 1:10 and 4:1. The ratio of fenofibrate to polymer in Curtet has greater than 7 times more fenofibrate to PVP than the claimed ratio of fenofibrate to polymer. There is simply no motivation in Curtet to drastically reduce the ratio used in Curtet to arrive at the claimed invention.

The PTO asserts that Applicants failed to show the criticality of the claimed ratio. Applicants respectfully disagree. Moreover, Applicants respectfully submit that the PTO has not established a *prima facie* case of obviousness for the reasons discussed above and that any "criticality" is irrelevant in view thereof. The case law cited by the PTO⁴ requires that the general conditions of a claim be disclosed in the prior art. In the present case, the claimed ratios are not a variation of or encompassed by the prior art. The claimed ratios are significantly different than the ratios recited in Curtet. In view of the above, Applicants respectfully submit that the PTO has not established a *prima facie* case of obviousness.

Although the criticality of the claimed range is not required because the PTO has not established a *prima facie* case of obviousness, Applicants have provided data showing the criticality of the claimed range, as discussed below.

Curtet corresponds to EP-A-0330532 which is discussed in the specification at page 2, lines 1-20 and Examples 2-4. Curtet corresponds to Lipanthyl® 200M in Figures 1 and 2 in the present application.

The dissolution medium and conditions in the present claims are a rotating blade method at 75 rpm, where the dissolution medium is water with 2% polysorbate 80 or water with 0.025 M sodium lauryl sulfate. In contrast, Curtet uses a rotating vane or continuous flow cell where the

³ Curtet at column 2, lines 30-40 and column 2, line 65 to column 3, line 5.

⁴ *In re Aller*, 220 F.2d 454 (1955).

dissolution medium is water with 0.1 M sodium lauryl sulfate. The dissolution medium of Curtet comprises much more sodium lauryl sulfate (i.e., surfactant) than the dissolution medium of the claimed invention. Having more surfactant will necessarily enhance dissolution. Accordingly, it is necessary to compare the composition described in Curtet and the claimed composition using the same method. This was done in the present application.

Applicants have shown in Example 2 and Figure 1 of the present application that the claimed invention has an unexpectedly superior dissolution profile compared to Lipanthyl® 200M as described by Curtet. For the Examiner's convenience, a comparison of the dissolution profile recited in the claims with the dissolution profile of Curtet (i.e., Lipanthyl® 200M) is shown in the Table below.

Time	% Dissolution of Claimed Invention described in Specification	% Dissolution by Inventive Example shown in Example 2 of the Application	% Dissolution by Curtet as Lipanthyl® 200M shown in Example 2 of the Application
30 minutes	at least 75%	95.9%	54.9%

As shown above, Example 2 and Figure 1 in the application demonstrate that Curtet does not have a dissolution profile like the dissolution profile having the claimed fenofibrate to polymer ratio. The claimed invention has an unexpectedly superior profile when compared to Curtet.

Applicants also refer to the Declaration under 37 CFR § 1.132 by Pascale Blouquin (the Blouquin Declaration)⁵ to show that the claimed invention has unexpectedly superior properties when compared to Curtet's dissolution profile shown in the Laboratory Notebooks submitted with the Blouquin Declaration. Blouquin Declaration at ¶ 14. A comparison of the pending claims (i.e., the dissolution which is achieved), the inventive example in the present application and Curtet (i.e., the dissolution data from Lot No. 2177 in the Laboratory Notebook No. 1 at Bates Number Fournier 1001569 is set forth in the table below). Blouquin Declaration at ¶ 14.

⁵ The Blouquin Declaration was submitted in the Information Disclosure Statement filed May 6, 2006.

Time	% Dissolution Achieved with Claimed Invention	% Dissolution by Inventive Example shown in Example 2 of the Application	% Dissolution by Curtet as Lipanthyl® 200M from Lot No. 2177 described in the First Blouquin Declaration and shown in Lab Notebook No. 1 at Fournier No. 1001569	% Dissolution by Curtet as Lipanthyl® 200M from Lot No. 2177 described in Example 2 of the Application
30 minutes	at least 75%	95.9%	67.7%	54.9%
60 minutes	--	--	78%	--

The claimed invention achieves 75% dissolution in 30 minutes, and Inventive Example 2 achieves 95.9% dissolution in 30 minutes. The data in the Laboratory Notebook submitted to the PTO shows that it takes 60 minutes for Curtet's Lipanthyl® 200M to achieve a dissolution of 78%. Blouquin Declaration at ¶ 15. In other words, it takes almost twice as long for Curtet's Lipanthyl® 200M to achieve a dissolution that the claimed fenofibrate composition can achieve in 30 minutes. Blouquin Declaration at ¶ 15. In view of these results, it is Ms. Blouquin's opinion that the claimed invention is superior to Curtet's Lipanthyl® 200M. Blouquin Declaration at ¶ 15.

Applicants respectfully submit that Curtet does not disclose or suggest a composition that exhibits such a dissolution profile with the claimed ratio of fenofibrate to polymer, and that Curtet provides no motivation or suggestion to produce the claimed ratio of fenofibrate to polymer in the composition. The dissolution profile that can be obtained with the claimed composition is unexpectedly superior when compared to Curtet. Accordingly, Curtet cannot render the claimed invention obvious.

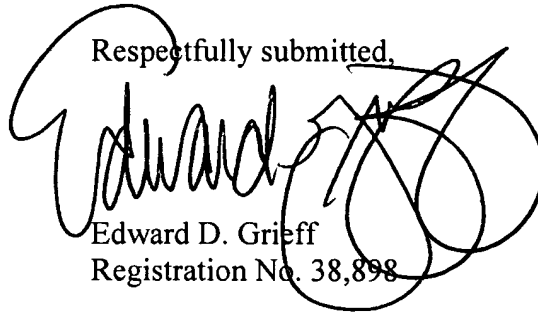
Curtet fails to provide any motivation for one skilled in the art to modify the fenofibrate to polymer ratio. Curtet is solely concerned with co-micronization, and provides no guidance as to the relevancy of the amount of fenofibrate or polymer. Hence, Curtet does not provide motivation to modify the ratio of fenofibrate to polymer to arrive at the claimed ratio.

Applicants respectfully submit that pending claims 16-55, 81 and 82 are unobvious over Curtet because the PTO has not established a prima facie case of obviousness and Applicants

have shown the criticality of the claimed range and respectfully request that the rejection under § 103 be withdrawn.

Summary

An early and favorable reconsideration and allowance of claims 16-55 and 81-82 is respectfully requested.

Respectfully submitted,

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